THE EFFECT OF LATE REIMMUNIZATION ON THE PRODUCTION OF ANTITUMOR ANTIBODIES

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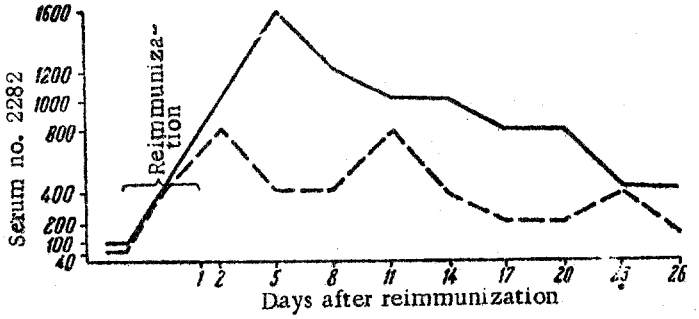
The effect of repeated immunization on the immunological reactivity of the body after a long interval is a well-studied problem in infection immunology. The work of a number of authors [1, 2, 3] has shown that in response to late reinjections of antigens the antibody production (precipitins, agglutinins) is considerably increased by comparison with the height of the titer after primary immunization.

So far as the immunization of animals with tumor material is concerned, however, this problem has so far received insufficient attention.

The aim of the present work was to ascertain the effect of late reimmunization with antigens from tissue of Ehrlich's tumor of mice on the production of antibodies after a long interval.



The course of antibody production in rabbits after reimmunization with antigens from tissue of an Ehrlich's mouse tumor.
---- complement fixation reaction with tumor antigen.
—— complement fixation reaction with spleen antigen.

EXPERIMENTAL METHOD

Primary immunization was undertaken with saline extracts of the tissue of an Ehrlich's mouse adenocarcinoma (ascitic form) by the shortest scheme of 4 injections every other day.

Experiments were carried out on rabbits. The animals were divided into 5 groups, each of 4 rabbits. The first group of animals received injections of 0.2 mg (as protein) of antigen per course of immunization, the second

— 2 mg, the third — 12 mg, the fourth — 40 mg and the fifth — 100 mg per course. The antigens were injected intravenously. The quantity of protein was determined by Conway's nitrogen method. On the 5th day after the last injection of antigens, and thereafter every third or fourth day for 2 months, blood was taken from all the rabbits and sera prepared.

The results of the serological analysis of the sera obtained after primary immunization were published previously [4].

The rabbits were reimmunized with antigens from the same tumor $4^1/_2$ months after the conclusion of the primary immunization. The antugens were also injected intravenously — 3 times on alternate days. The first group received 0.15 mg (as protein) per course of reimmunization, the second — 1.5 mg, the third — 9 mg, the fourth — 30 mg and the fifth — 75 mg. On the day before the beginning of injection of the antigens, on the day after the beginning of reimmunization and thereafter every third or fourth day for one month, blood was again taken and sera prepared for serological analysis.

The serological analysis of all the sera thus obtained was made by means of the classical complement fixation reaction at 37°.

EXPERIMENTAL RESULTS

Tests of the sera obtained by means of the complement fixation reaction showed that all the rabbits produced antitumor antibodies to roughly the same degree after reimmunization.

For instance, in the sera of animals reimmunized with antigens in a dose of 0.15 mg per course, the titer of antitumor antibodies varied from 1:1000 "++" to 1:1600 "++". In the sera of the animals of the second group reimmunized with antigens in a dose of 1.5 mg, the antibody titer varied within the same limits. In all the remaining groups of reimmunized animals, the titer of antitumor antibodies was roughly equal to the titer in the sera of the first 2 groups of rabbits.

In these experiments we were thus unable to detect any relationship between the immunological reactivity (the production of antitumor antibodies) and the doses of antigens injected, as was observed after the primary immunization.

Attention should be drawn to the fact that the titer of antitumor antibodies was twice as high after reimmunization as after primary immunization.

It is also interesting to observe that an increase in the titer of antitumor antibodies was found after reimmunization in all the animals. From an inspection of the course of production of anti-tumor antibodies, we noted that the growth of the antibody titer after reimmunization took place more rapidly than at the end of primary immunization. For instance, whereas after primary immunization the highest titer of antitumor antibodies was observed on the 9th-14th day, after reimmunization it reached its highest level on the 5th-8th day. For a clearer illustration of the course of antibody production, in the figure we show the most typical curve. The points on the curve indicate the complement fixation reaction with an intensity of "++". In order to determine the specificity of the sera obtained, the complement fixation test was set up not with antigens from tumor tissue, but also with antigens from liver and spleen tissue from normal mice. The curves depict the reaction with antigens from spleen tissue only, as being closest in an antigenic respect to tumor.

Besides the accelerated antibody production already mentioned, the figure also shows that there are moments in the formation of antibodies when the titer of antitumor antibodies considerably exceeds the titer of antibodies against antigens from normal spleen.

Our findings show that after late reimmunization with antigens from tumor tissue, the titer of antitumor antibodies is considerably higher, and their rate of production is more rapid than after primary immunization.

It was also found that, irrespective of the dose of antigens, in our experiments all the rabbits reacted to roughly the same degree after reimmunization.

The increase in the immunological reactivity of animals after late reimmunization with antigens from Ehrlich's mouse tumor (ascitic form), which we observed, corresponds to the results obtained in infectious immunology. In this connection it may be postulated that laws governing the relation between the immunological

reactivity of the animal and late reimmunization, which have been demonstrated in infectious immunology, are also of great importance in the immunization of animals with tumor material.

SUMMARY

This work deals with the effect of remote reimmunization of rabbits with antigens of the tissue of mice Ehrlich's tumor on the production of the antitumor antibodies. The data obtained demonstrate that following remote reimmunization with antigens of the tumor tissue the titer of the antitumor antibodies was considerably higher and the velocity of their production was greater that after primary immunization. After the second immunization all the rabbits reacted in about the same way, regardless of the antigen dose.

LITERATURE CITED

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* Original Russian pagination. See C. B. Translation.